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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/776,865	Applicant(s) HELLERQVIST, CARL G.	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *2,17-28,49-54,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-16,29-48,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-58* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The election with traverse filed June 21, 2002 in Paper No. 5 is acknowledged and has been entered. Applicant has elected group 1, claims 1, 3-16, 29-48, 55, and 56, insofar as the claims are drawn to a method for preventing cancer in a mammal. Furthermore, Applicant has elected the species of invention in which at least one immunogenic fragment having substantial identity to Hab3 is administered, the method by which the amount of said immunogenic fragment is administered is subcutaneous injection, the adjuvant of which the immunogenic composition is composed is Freund's adjuvant, and the protein carrier to which the GBS toxin receptor or fragment thereof is conjugated or linked is keyhole limpet hemocyanin (KLH).

2. Claims 1-58 are pending in the application. Claims 2, 17-28, 49-54, 57, and 58 have been withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

3. Claims 1, 3-16, 29-48, 55, and 56, insofar as the claims are drawn to elected invention are currently under prosecution.

Election/Restrictions

4. Applicant's election with traverse of group 1, claims 1, 3-16, 29-48, 55, and 56, insofar as the claims are drawn to a method for preventing cancer in a mammal in Paper No. 5 is acknowledged.

The traversal is on the ground(s) that MPEP § 803 states that an entire application should be examined on the merits, including claims drawn to distinct or independent inventions, provided that doing so would not be a serious burden and note that many of the inventions are identically classified. In addition, Applicant has traversed the requirement to elect a species of invention, arguing that the members of

the Markush groups are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden.

Applicants' arguments have been carefully considered but have not been found persuasive. The classification is but one indication of the subject matter to which the claims are drawn, and in this instance, the search required to examine any one group or species of invention is not co-extensive with that required to examine any other group or species. Therefore, the examination of more than one group or species of invention would constitute a serious burden. Accordingly, the restriction and election requirement is deemed proper and therefore made final.

Specification

5. The use of the numerous trademarks has been noted in this application. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of an improperly demarcated trademark appears on page 23.

Claim Objections

6. Claims 1, 3-16, 29-48, 55, and 56 are objected to because of the following informalities:

(a) Claims 1, 3-16, 29-48, 55, and 56 are objected to because the claims are drawn in the alternative to the subject matter of non-elected inventions. Appropriate correction is required.

(b) Claim 16 is objected to because the Markush group is improperly constructed. Appropriate correction is required.

Claim R jections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 3-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being reasonably enabling for a method for preventing melanoma in mice immunized with "HP59/CFA", does not reasonably provide enablement for a method for preventing cancer in a mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 30-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being reasonably enabling for a composition consisting of a mixture of Hab1, Hab2, and Hab3, or alternatively consisting of a mixture of p55a, p56a, p57a, Hab1, and Hab2 for attenuating tumor burden in mice challenged with melanoma or Lewis lung tumor cells and reasonably enabling for a method for protecting against the development of melanoma in mice immunized with "HP59/CFA", does not reasonably provide enablement for a composition for protecting against or attenuating cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a composition consisting of a mixture of Hab1, Hab2, and Hab3, or alternatively consisting of a mixture of p55a, p56a, p57a, Hab1, and Hab2 for attenuating tumor burden in mice challenged with melanoma or Lewis lung tumor cells and reasonably enabling for a method for producing a composition consisting of "HP59/CFA" for protecting against the development of melanoma in mice, does not reasonably provide enablement for a

method for producing a composition for treatment and/or prevention of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1 and 3-16 are drawn to a method for preventing cancer in a mammal. Claims 30-48 are drawn to a composition for protecting against or attenuating cancer. Claims 55 and 56 are drawn to a method for producing a composition for treating and/or preventing cancer.

The specification discloses, "a vaccine or method is said to "prevent" or "protect against" a medical condition if its administration to an individual results in the failure of the individual to develop the medical condition" (page 6, lines 31-33). The specification discloses, "a vaccine or method is said to [...] "attenuate" [...] a medical condition if its administration to an individual results in the suppression or partial suppression of at least one symptom or other manifestation of the medical condition in the individual" (page 7, lines 1-4).

The specification shows that mice immunized with a mixture of particular antigenic fragments of SP55 and/or HP59 tend to have smaller tumor burdens than mice immunized with adjuvant alone following challenge with either melanoma or Lewis lung tumor cells. In addition, the specification shows that mice immunized with "HP59/CFA" survive longer than mice immunized with "CFA" following challenge with melanoma cells.

However, considering the state of the art and the high level of unpredictability associated with the art, the amount of exemplification provided in the specification is not reasonably commensurate in scope with claims to enable the skilled artisan to make and use the claimed invention with a reasonable expectation of success without having need to perform additional, undue experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples,

the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

Clinically, the protection of patients against the development of cancer has proven intractable and a therapeutic benefit of administering cancer vaccines has been rarely observed. Bodey, et al (*Anticancer Research* **20**: 2665-2676, 2000) teach, "while cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy" (page 2665, column 2). As to the current state of the art, Bodey, et al comment, "the use of active specific immunotherapy (ASI) for cancer (cancer 'vaccines') is still in its scientific infancy despite several decades of clinical and basic research" (page 2668, column 2). Thus, little has changed to alter the artisans' expectations of the still prospective immunotherapy since the invention was made. Cox, et al (*Science* **264**: 716-719, 1994) teach, "neither adoptive transfer of melanoma-specific CTLs nor specific active immunotherapy with whole melanoma cells or cell-derived preparations has led to the eradication of melanoma in more than a minority of patients" (page 716, column 2). Then again, even that small note of promise has since faded. Bodey, et al disclose, "ASI in at least one instance may have cured melanoma in a patient with metastatic disease, but that patient developed another immunologically and genetically distinct melanoma" (page 2668, column 2). In the abstract Bodey, et al speculate upon the reasons that ASI is ineffective or lacks efficacy:

> The theoretical basis for all of these approaches is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the target antigens contained with a cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs [tumor associated antigens] in the context of the particular human leukocyte antigen (HLA) subclass and the necessary

costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use.

The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (*Journal of NIH Research* **7**: 46-49, 1995) states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph). Ezzell, et al further teaches that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micro-metastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (page 48, paragraph 6). More recently, Bodey, et al (cited supra) state, "there should be caution about assuming that a single epitope or even a few epitopes combined will be as effective 'crude' materials, which might better be thought of as 'polyvalent'" (page 2668, column 2). Spitler (*Cancer Biotherapy* **10**: 1-3, 1995) recognizes the lack of predictability of the nature of the art when she states, "ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: 'cancer vaccines don't work'. Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response" (page 1, paragraph 1).

Whatever avenue the artisan takes, in view of the unpredictability in the art, the rarity and lack of uniformity in the successful application, and the numerous and substantial limitations encountered, the threshold of enablement is high. The specification must enable one of skill in the art to make and to use the invention with a reasonable expectation of success. To have success, the use of the invention must elicit a melanoma-specific CTL response against the antigen. Boon (*Advances in Cancer Research*, 1992, **58**: 177-210) teaches that for successful application of active immunization in human patients, we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have already occurred in the patient and in such cases, active specific immunization will be fruitless, since anergic TCL cannot be activated, will not proliferate,

and are deficient in effector function. Several lines of evidence suggest that large tumor burdens can tolerize, or at least depress the capability to respond against the tumor (page 206, paragraph 2). Furthermore, among other mechanisms, Arceci (*Journal of Molecular Medicine* **76**: 80-93, 1998) teaches, "it has been hypothesized that tumor cells may escape immune recognition and subsequent killing by failing to satisfy one or more of the [...] requirements for T cell antigen recognition and activation. For example, if antigen presentation does not occur because of low or absent expression of MHC or lack of a recognizable tumor antigen, then tumor cells would not be recognized" (page 83, column 2). Areci continues, "on the other hand, if antigen recognition occurs by T cells but tumor cells do not express a costimulatory molecule, then T cells might become anergic to the tumor cells" (page 83, column 2). Notably, Areci teaches, "most solid tumors usually do not express costimulatory molecules" (page 84, column 1); therefore, it is unlikely that use of the invention can effectively immunize a patient against cancer, or more particularly melanoma.

There is considerable art indicating that cancer vaccines are ineffective, *even if antigen-specific T-lymphocytes can be activated by immunization protocols*. Lee, et al (*Journal of Immunology* **163**: 6292-6300, 1999) teach, "although comparative ex vivo sensitization of pre- and postvaccination PBMC [peripheral blood mononuclear cells, such as B- and T-lymphocytes] has identified reproducible, vaccine-specific systemic T cell responses to immunization, in the majority of cases no regression is seen" (page 6292, column 1). In studies similar to those that are set forth in the examples in the specification, Lee, et al teach that melanoma antigen epitopes were identified and that these peptide epitopes were capable of inducing highly specific T cell responses against autologous and some HLA-matched tumor cells. Lee, et al disclose that "these studies gave the impression that vaccines induce powerful immunizations comparable to those demonstrable against common pathogens such as the influenza virus to which individuals are repeatedly exposed throughout their lifetime". However, "in most cases, this **vaccine-induced T cell reactivity still does not lead to tumor regression**" (emphasis added) (page 6299, column 1). One of the reasons for the discrepancy, Lee, et al suggest, may be that in vitro methods, which are commonly used to assess

immune post-vaccination immune response, such as cell-mediated cytotoxicity assays, tend to "overestimate quantitatively the strength of the immune reaction within the organism" (page 6299, column 1). Lee, et al catalog a variety of possible explanations for the lack of efficacy, including clonal deletion, exhaustion, or senescence, which are implicated in the development of systemic, epitope-specific immune tolerance, and inadequate immune response attributable to decreased T cell receptor signaling capacity or circulating immune-suppressive cytokines, but conclude that their data suggest that the extent rather than the quality of the response might be more significant limitation of the vaccination protocol (page 6299, column 2). More specifically, Lee, et al report, "we were surprised at the relatively low numbers of CTL precursors after vaccination even in patients' samples that boasted an exceptional epitope-specific expansion in vitro" (page 6299, column 2). Lee, et al summarize their study, teaching that "a peptide-based vaccine can effectively generate a quantifiable T cell-specific immune response in the PBMC of cancer patients, though such a response does not associate with a clinically evident regression of metastatic melanoma" (abstract). While Lee, et al refer specifically to the treatment of melanoma using a different epitope, the teachings are highly germane to the enablement issues relevant in the instant application, because the severe limitations will undoubtedly be shared by any protocol that uses the claimed invention, and there is no exemplification in the specification that would suggest otherwise. In yet another example, Zaks, et al (*Cancer Research* **58**: 4902-4908, 1998) teach that immunization of patients diagnosed with cancer with a peptide epitope derived from the tumor antigen HER-2/neu/ErbB2 leads to activation of peptide-specific cytotoxic T-lymphocytes, but that the T-lymphocytes fail to recognize tumor cells that express the antigen. Zaks, et al disclose that their experience is not unique (page 4907, column 2). Gao, et al (*Journal of Immunotherapy* **23**: 643-653, 2000) found that although antitumor CTL response was enhanced by immunization, the tumors failed to regress. Gao, et al teach that the lack of regression was associated with a lack of CTL migration to the tumor sites (abstract). Thus, activation of peptide epitope-specific CTL is not an appropriate endpoint and a prediction or estimation of efficacy based only upon such data is imprudent or inexact.

Moreover, many attempts to provide efficacious therapeutic or prophylactic immunotherapy for cancer patients have paradoxically failed despite evidence of that vaccination has induced proliferation of tumor antigen-specific CTL, as no major protective antitumor response was seen in these cases. There are many reasons that the promise of pre-clinical endeavors is broken once clinical trials ensue. Among the possible reasons, with regard to animal models, tumors tend to be highly immunogenic and thus quite unlike most human cancers. Gura (*Science* **278**: 1041-1042, 1997) discusses the limitations of animal and cell models. Gura teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but that only 39 have actually been shown to be useful for chemotherapy (page 1041, first and second paragraphs). Sadly, Gura reports that using xenograft animal models to evaluate the potential of novel antitumor therapies often leads to the discovery of " 'good mouse drugs rather than good human drugs' " (page 1041, column 2), because the results acquired using animal models or cell culture are not correlative with those acquired in the clinic. Additionally, with regard to lack of correlation, Lee, et al (cited supra) caution, "it is likely that the immune responses judged after ex vivo expansion of postvaccination PBMC overestimate quantitatively the strength of the immune reaction within the organism" (page 6299, column 1). The magnitude of the immune response that might be sufficient to protect a mammal against a tumor is unknown. Finally, Bodey, et al teach that despite promising, even tantalizing results *in vitro* and *in vivo*, especially with animal models, the failure of cancer vaccines is predicated by very relationship between the tumor and the host immune system, which effectively makes the use of cancer vaccines futile:

> Malignant tumors undergo constant microevolution. Natural selection of the most advantageous surface IP [immunophenotype] involves constant modulation of previous IPs. Progressive dedifferentiation characterizes all neoplastically transformed cells. During this process, numerous 'novel' cell surface antigens appear, are modified and thus do not present the host's immune system with some immunogenic elements. The leukocytic inflammatory infiltrate contains cells with divers capabilities including neutrophils, macrophages and other professional APCs [antigen-presenting cells], as well as T lymphocytes. In situ activation of TAA [tumor-associated antigen] specific CTL [cytotoxic T-lymphocyte] clones occurs and thousands of tumor cells are lysed. However, as we would expect from any population in danger of extinction, the cells of the neoplastically transformed mass proceed with their microevolution and numerous clones

> of tumor cells survive each repeated attack by the immune system through secretion of immunoinhibitory cytokines, downregulation of MHC molecules, loss of costimulatory molecules, and induction of clonal T cell anergy, among other as yet uncovered ways. This process continues until the 'creation' (ironically as it may sound, by the host's immune system) of highly resistant, poorly immunogenic, and extremely aggressive clones of tumor cells. This is the reality of cancer progression: a back-and-forth struggle between host and tumor, with evolutionary dynamic exchanges throughout the entire process. Use of cancer vaccines to stimulate the immune system may be in vain" (citations omitted) (pages 2673-2674).

In summary, because of the demonstrated unpredictability in the art of cancer immunotherapy, in the absence of guidance, direction, and exemplification that is reasonably commensurate in scope with the claims, one skilled in the art could not make and use the claimed method with a reasonable expectation of success without having need to perform additional, undue experimentation. Therefore, the specification fails to provide an enabling disclosure, as would be required for patentability under 35 USC § 112, first paragraph.

9. Claims 1, 3-16, 29-48, 55, and 56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 3-16 are drawn to a method for preventing cancer in a mammal, wherein said method comprises administering to said mammal an amount of one or more GBS toxin receptors. Claims 29-48 are drawn to a composition comprising one or more GBS toxin receptors, and claims 55 and 56 are drawn to a method for producing a composition comprising at least one GBS toxin receptor.

However, the specification is not sufficient to meet the written description requirement set forth under 35 USC § 112, first paragraph because the specification does not describe a representative number of the members of the genus of GBS toxin receptors to which the claims refer. The specification describes HP59 and SP55, which are polypeptides that function as receptors of a group B Streptococcal (GBS) toxin, namely the type III capsular polysaccharide or CM101. However, the specification does

not adequately describe any other receptor of any other GBS toxin, and therefore the skilled artisan given the benefit of Applicant's disclosure, could not immediately recognize at least a substantial number of the members of the genus of GBS toxin receptors to which the claims refer. For example, the specification does not describe the receptor(s) that bind β-hemolysin. Accordingly, the specification does not describe the invention in such a way so as to reasonably convey to the skilled artisan that the Applicant had possession of the invention at the time the application was filed.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, 3-16, 29-48, 55, and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3-16 are indefinite because claim 1 does not recite a positive process step that clearly relates back to the preamble of the claim. Because the claim lacks a positive process step, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention since it is not evident that each and every step that Applicant regards as essential in practicing the method to meet the objective stated in the preamble is recited in the body of the claim. Amending claim 1 to recite, for example, the phrase "whereby the development of said pathoangiogenic condition in the mammal is prevented" at the end of the last line of the claim can obviate this ground of rejection without altering the scope of the claim.

Claims 1, 3-16, 29-48, 55, and 56 are indefinite because the claims use "GBS" to designate "Group B β-hemolytic Streptococci". The use of an acronym to identify the subject matter to which the claims are drawn renders the claims indefinite because others may use the same acronym to designate non-identical or dissimilar subject matter. Amending claim 1 to recite, for example, "Group B β-hemolytic Streptococcal (GBS)" can obviate this ground of rejection.

Claims 2-14 and 40-48 are indefinite because claims 4, 6-9, 11-14, 40, 42-45, 47, and 48 recite the term "substantial". The term is a relative term that is not defined in the claims. In addition, the specification does not provide a standard for ascertaining the degree to which the claims require the polypeptides or fragments to be identical. Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Deleting "substantial" in claims 4, 6-9, 11-14, 40, 42-45, 47, and 48 can obviate this ground of rejection.

Claims 7, 14, 44, and 48 are indefinite because the claims use of the designations "Hab1", "Hab2", "Hab3", "Hab4", "p55a", "p56a", and "p57a" as the sole means of identifying the polypeptides to which the claims refer. The use of a laboratory designation only to identify a particular polypeptide renders the claims indefinite because different laboratories may use the same laboratory designation to define a completely distinct polypeptide. Amendment of the claims to include the amino acid sequence of the polypeptide by reference to a specific sequence identification number of an amino acid sequence set forth in the Sequence Listing can obviate this rejection, because the amino acid sequence of a polypeptide is a unique identifier that unambiguously defines a given polypeptide. For example, amending claim 7 to recite "wherein the at least one immunogenic fragment has identity to the polypeptide consisting of amino acid residues 8-28 of SEQ ID NO: 2 (Hab3)" and similarly amending the other claims can obviate this ground of rejection.

Claims 55 and 56 are indefinite because claim 55 does not recite a positive process step that clearly relates back to the preamble of the claim. Because the claim lacks a positive process step, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention since it is not evident that each and every step that Applicant regards as essential in practicing the method to meet the objective stated in the preamble is recited in the body of the claim. Amending claim 55 to recite, for example, the phrase "whereby the said composition is produced" at the end of the last line of the claim can obviate this ground of rejection without altering the scope of the claim.

Claim R j ctions - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
>
> > (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> >
> > (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

13. Claims 1, 3-7, 15, 16, 29-34, 37, 39-41, 43, 44, 55, and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Nair, et al (*International Journal of Cancer* **70**: 706-715, 1997).

Nair, et al teach a method for treating a mammal, wherein said method comprises immunizing the mammal with a composition comprising antigen-presenting cells pulsed with tumor extracts.

The methods and composition of the prior art are deemed that same as the methods and composition to which the claims are drawn absent a showing of any difference. The Office, however, does not have the facilities for examining and comparing Applicant's product and methods with the product and methods of the prior art in order to establish that the product of the prior art do not possess the same material, structural, and functional characteristics of the claimed product, or that the methods of the prior art do not produce the same effect or product as the claimed

methods. In the absence of evidence to the contrary, the burden is upon the Applicant to prove that the claimed product and methods are functionally different than those taught by the prior art and to establish patentable differences.

Conclusion

14. No claims are allowed.

15. The prior art made of record and not relied upon is considered pertinent to Applicants' disclosure. Bocchia, et al reviews the state of the art of antitumor vaccination. Moriguchi, et al teach a method for producing and using a vaccine comprising tumor cells. Hellerqvist, et al (1996) teach the modulation of interleukin-12 mRNA expression in leukocytes of cancer patients treated with CM101. Hellerqvist, et al (1993) teach the antitumor effects of a GBS toxin, namely the polysaccharide exotoxin from type III group B β-hemolytic streptococci. Edwards, et al teach that capsular polysaccharide regulates neutrophil complement receptor interactions with type III group B streptococci. Henneke, et al teach the engagement of CD14 and multiple toll-like receptors by group B streptococci. Fu, et al teach the identification of a novel membrane protein, HP59, with therapeutic potential as a target of tumor angiogenesis.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
October 4, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600